



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NO 7539 <i>WO</i>		FOR FURTHER ACTION	See Form PCT/PEA416
International application No. PCT/EP2004/006614	International filing date (<i>day/month/year</i>) 18.06.2004	Priority date (<i>day/month/year</i>) 23.06.2003	
International Patent Classification (IPC) or national classification and IPC A23L1/29, A23L1/30, A23L1/305, A61K35/74			
Applicant NESTEC S.A. et al			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 9 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> <i>sent to the applicant and to the International Bureau</i> a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 19.01.2005		Date of completion of this report 04.10.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016		Authorized Officer De Jong, E Telephone No. +31 70 340- 	

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-21 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 15-21(partly)
because:
 - ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☒ no international search report has been established for the said claims Nos. 15-21(partly)
 - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
 - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
 - ☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-14
	No: Claims	15-21
Inventive step (IS)	Yes: Claims	
	No: Claims	1-21
Industrial applicability (IA)	Yes: Claims	1-14
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Ad III

Claims 15-21 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

The search was based on the alleged effects of the composition, thus, an opinion on novelty and inventive step was also based on these alleged effects (see below).

Ad V

1. Reference is made to the following documents:

- D1: EP-A-1 048 226 (NESTLE SA) 2 November 2000 (2000-11-02)
- D2: US-A-5 916 621 (SAWATZKI GUENTHER ET AL) 29 June 1999 (1999-06-29)
- D3: EP-A-1 228 707 (CAMPINA MELKUNIE BV) 7 August 2002 (2002-08-07)
- D4: US 2003/077255 A1 (SABHARWAL HEMANT K) 24 April 2003 (2003-04-24)
- D5: EP-A-0 904 784 (NUTRICIA NV) 31 March 1999 (1999-03-31)
- D6: WO 02/15719 A (NESTLE SA) 28 February 2002 (2002-02-28)
- D7: US 2003/017192 A1 (KANAFANI HANNY ET AL) 23 January 2003 (2003-01-23)
- D8: OGATA T ET AL: "EFFECT OF BIFIDOBACTERIUM LONGUM BB536 YOGHURT ADMINISTRATION ON THE INTESTINAL ENVIRONMENT OF HEALTHY ADULTS" MICROBIAL ECOLOGY IN HEALTH & DISEASE, CHICHESTER, GB, vol. 11, no. 1, March 1999 (1999-03), pages 41-46, XP009023764
- D9: GRILL J P ET AL: "Bifidobacteria and probiotic effects: action of Bifidobacterium species on conjugated bile salts." CURRENT MICROBIOLOGY 1995 CORRESPONDENCE (REPRINT) ADDRESS, J. BALLONGUE, LAB. DE CHIMIE BIOL., INST. HENRY TISSIER, UNIV. DE NANCY I, BP 239, 54506 VANDOEUVRE LES NANCY, FRANCE, vol. 31, no. 1, 1995, page 23, XP002298116
- D10: ISOLAURI E ET AL: "Probiotics in the management of atopic eczema" CLINICAL AND EXPERIMENTAL ALLERGY, vol. 30, no. 11, November 2000 (2000-11), pages 1604-1610, XP002298117 ISSN: 0954-7894
- D11: WO 02/060276 A (MAEYRAE-MAEKINEN ANNIKA ; SUOMALAINEN

- D12: TARJA (FI); VALIO LTD (FI); VAAR) 8 August 2002 (2002-08-08)
SAXELIN M: "LACTOBACILLUS GG - A HUMAN PROBIOTIC STRAIN
WITH THOROUGH CLINICAL DOCUMENTATION" FOOD REVIEWS
INTERNATIONAL, NEW YORK, NY, US, vol. 13, no. 2, 1997, pages
293-313, XP000199732
- D13: KALLIOMAKI M ET AL: "Probiotics and prevention of atopic disease: 4-
year follow-up of a randomised placebo-controlled trial" LANCET THE,
LANCET LIMITED. LONDON, GB, vol. 361, no. 9372, 31 May 2003
(2003-05-31), pages 1869-1871, XP004428374 ISSN: 0140-6736
- D14: US 2002/004527 A1 (O' CONNOR DEBORAH L ET AL) 10 January
2002 (2002-01-10)

2. An infant formula containing sweet whey protein from which CGMP has been removed, was known in the art:

D1 discloses (see claims 1-4) an infant formula, comprising a protein source, which comprises 97-98.5% of hydrolysed whey from which CGMP has been removed. It also contains a lipid source, among which e.g. fish oil (see Examples 1-2). It is stated (see p.2 par.0007) that sweet whey from which CGMP has been removed has a reduced threonine content and an increased tryptophan content and is therefore suitable as a protein source for infants. Furthermore, the whey fraction is hydrolysed to prevent allergic reactions in infants at risk and to make the protein easier to digest (p.3 par.0018. D1 is especially relevant for the subject-matter of claims 1, 2, 9 and 11-13. D2 discloses a whey protein dominant baby food, wherein the whey protein is obtained from sweet whey in which the protein content has been modified by the selective removal of at least a portion of the GMP therefrom (claim 1). In Example 2 a food is prepared, containing, based on total protein, 55% GMP reduced whey protein hydrolysate. It is stated in col.1 l.28-31 that there is a need to adapt the constituents of formulas as much as possible to the composition of human milk. D2 is especially relevant for the subject-matter of claim 1.

D3 teaches (see claims 1-10) the use of α -lactalbumin as a prebiotic food (additive) and as a pharmaceutical composition for the treatment of gastroenteritis. A food product would preferably contain 10-40 w/w% of α -lactalbumin, based on the protein part (claim 4). On p.2 par.0005 it is disclosed that it has been shown that α -lactalbumin and α -lactalbumin enriched whey protein concentrate have improved prebiotic properties compared to whole whey. " α -Lactalbumin" is considered to fall under the definition "modified sweet whey proteins comprising no CGMP". D3 is especially

relevant for the subject-matter of claims 1 and 8.

D4 is directed (see p.2 par.0014) to a composition (e.g. infant formula), comprising bifidobacteria and substantially purified monomeric α -lactalbumin. The composition may also contain a lactic acid bacterial strain, e.g. *Streptococcus thermophilus* (claims 1-12). On p.1 par.0003 it is disclosed that the benefits of probiotics include enhanced host defence to disease, improving colonisation resistance of harmful micro flora and favouring the formation of a well-balanced, indigenous, intestinal micro flora in newborn children. Par.0007 teaches that multimeric α -lactalbumin has been shown to provide anti-bacterial effects and par.0010 (p.2) that the claimed compositions provide a synergistic anti-bacterial effect against a broad spectrum of microorganisms. D4 is especially relevant for the subject-matter of claims 1 and 3.

The use of probiotics in infant formula was also known:

See D4 above.

D5 discloses (Example 7) an infant formula with probiotics. Claim 2 lists *Bifidobacterium lactis*. In col.8 par.0058-col.9 par.0064 a whole range of positive effects of the use of probiotics is listed, among which therapy or prophylaxes of all kinds of disorders of the gastrointestinal tract. D5 is especially relevant for the subject-matter of claims 1 and 3.

D6 discloses in Example 6 a pediatric powder, containing *B. bifidus* and *S. thermophilus*. D6 is especially relevant for the subject-matter of claims 1 and 3.

D7 discloses (Example 3) a ready-to-use infant formula containing *Bifidobacterium lactis*. On p.1 par.0005 and 0006 various health benefits of probiotics are listed. D7 is especially relevant for the subject-matter of claims 1 and 3.

D8 teaches that yoghurt supplemented with *Bifidobacterium longum* BB536 has a beneficial effect on the intestinal environment of healthy adults. D8 is especially relevant for the subject-matter of claims 4, 7 and 15-21.

In D9 it is concluded that *Bifidobacterium longum* BB536 makes a good candidate for use in probiotic products. D9 is especially relevant for the subject-matter of claims 4, 7 and 15-21.

D10 discloses an infant formula, containing extensively hydrolysed whey and *Lactobacillus* GG (ATCC 53103), which improves skin conditions related to eczema. D10 is especially relevant for the subject-matter of claims 5-7 and 15-21.

D11 discloses a probiotic combination comprising different combinations of lactobacilli, propionic acid bacteria and/or bifidobacteria. The combination can be applied in food products, e.g. children's food (p.11 l.15-25) and is said to stimulate the immune system and general health (p.11 l.6-14). *Lactobacillus rhamnosus* ATCC 53102 is one of the

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preferred strains (claims 1-14). D11 is especially relevant for the subject-matter of claims 5-7 and 15-21.

D12 discloses the use of Lactobacillus GG (ATCC 53103) in various food products as a probiotic, having prophylactic and therapeutical effects. D12 is especially relevant for the subject-matter of claims 5-7 and 15-21.

D13 teaches that perinatal administration of Lactobacillus GG (ATCC 53103) reduces incidence of atopic eczema in at-risk children. D13 is especially relevant for the subject-matter of claims 5-7 and 15-21.

D14 discloses an infant formula, comprising DHA and ARA (see claims 1-21), especially for preterm infants up to a corrected age of 12 months, to enhance neurological development. D8 is especially relevant for the subject-matter of claims 1, 12 and 13.

3. The subject-matter of claims 1-14 is considered to be novel (Article 33(2) PCT), because none of the cited documents discloses an infant formula, containing both a probiotic and sweet whey proteins comprising no or reduced CGMP in an amount of at least 40% of the proteins.

However, the subject-matter of claims 1-14 is not considered to involve an inventive step (Article 33(3) PCT):

Closest prior art can be either one of D1-D4. The underlying technical problem to be solved over the closest prior art could have been the improvement of the infant formula, e.g. a further adaptation of formula to the composition of mother's milk. The finding that the use of probiotics gives a better product is not considered to involve an inventive step, because the use of probiotics in infant formula was known in the art, see D4-D7 and D10-D12.

Dependent claims 10 and 14 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT with respect to inventive step.

4. The subject-matter of claims 15-21 concerns a method for treatment of the human body by therapy. Consequently, these claims do not meet the requirements of Rule 67.1(iv) PCT. See also the PCT Preliminary Examination Guidelines 9.08-9.10.

Regarding the medical uses of the claimed composition, the following medical

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applications are not considered to be new or to involve an inventive step:

- claim 15: promoting physical development: whey from which CGMP has been removed provides a better protein source for infants (see D1-D4), thus, "promoting physical development" is not surprising;
- claim 18: improving gastro-intestinal comfort: the effects of probiotics were well-known in the art (see D4, D5, D8-D13);
- claim 20: developing a healthy gut micro flora: the effects of probiotics were well-known in the art (see D4, D8-D13).